IN THE CLAIMS:

Please cancel claims 2-4, 10-15, 20, 24-39, 41-42, 45, 75- 138, 145-278, 280-305, 309-314 and 317-331 without prejudice or disclaimer. Please amend claims 1, 5-9, 23, 46 and 279. Please add new claims 332-343. This listing of claims replaces all prior listings of claims.

LISTING OF CLAIMS:

1. (Currently amended) A modified interferon alpha cytokine that exhibits increased resistance to proteolysis compared to the unmodified cytokine~~; or a modified cytokine selected from the group consisting of modified cytokines comprising a sequence of amino acids set forth in any of SEQ ID NOS: 2-181, 233-1303 or a structural homolog thereof~~.

2-4. (Canceled)

5. (Currently amended) The modified cytokine of claim 1, ~~that is an~~ wherein the unmodified interferon alpha cytokine is selected from among interferon α-2b (IFNα-2b), interferon α-2a (IFNα-2a), interferon α-2c (IFNα-2c), [[or]] and an interferon having the sequence set forth in SEQ ID NO: 232.

6. (Currently amended) A modified cytokine of claim [[4]] 1, that is IFNα-2b or IFNα-2a or IFNα-2C selected from among proteins comprising one or more single amino acid replacements ~~in SEQ ID NOS: 1 or 182,~~ corresponding to the replacement in SEQ ID NOS: 1 or 182 of: L by V at position 3; L by I at position 3; P by S at position 4; P by A at position 4; R by H at position 12; R by Q at position 12; R by H at position 13; R by Q at position 13; M by V at position 16; M by I at position 16; R by H at position 22; R by Q at position 22; R or K by H at position 23; R or K by Q at position 23; F by I at position 27; F by V at position 27; L by V at position 30; L by I at position 30; K by Q at position 31; K by T at position 31; R by H at position 33; R by Q at position 33; E by Q at position 41; E by H at position 41; K by Q at position 49; K by T at position 49; E by Q at position 58; E by H at position 58; K by Q at position 70; K by T at position 70; E by Q at position 78; E by H at position 78; K by Q at position 83; K by T at position 83; Y by H at position 89; Y by I at position 89; E by Q at position 96; E by H at position 96; E by Q at position 107; E by H at position 107; P by S at position 109; P by A at position 109; L by V at position 110; L by I at position 110; M by V at position 111; M by I at position 111; E by Q at position 113; E by H at position 113; L by V at position 117; L by I at position 117; R by H at position 120; R by Q at position 120; K by Q at position 121; K by T at position 121; R by H at position 125; R

by Q at position 125; L by V at position 128; L by I at position 128; K by Q at position 131; K by T at position 131; E by Q at position 132; E by H at position 132; K by Q at position 133; K by T at position 133; K by Q at position 134; K by T at position 134; Y by H at position 135; Y by I at position 135; P by S at position 137; P by A at position 137; M by V at position 148; M by I at position 148; R by H at position 149; R by Q at position 149; E by Q at position 159; E by H at position 159; L by V at position 161; L by I at position 161; R by H at position 162; R by Q at position 162; K by Q at position 164; K by T at position 164; E by Q at position 165; [[and]] E by H at position 165,

wherein residue 1 corresponds to residue 1 of the mature IFNα-2b or IFNα-2a cytokine set forth in SEQ ID NOS:1 or 182.

7. (Currently amended) The modified cytokine of claim 6, wherein:

the protein is human;

has more resistance to proteolysis than the unmodified protein; and

the ~~protein~~ modified cytokine ~~is selected from proteins comprising~~ has one or more single amino acid replacements corresponding to replacements in SEQ ID NOS:1 or 182~~, corresponding to~~ of: F by V at position 27; R by H at position 33; E by Q at position 41; E by H at position 41; E by Q at position 58; E by H at position 58; E by Q at position 78; E by H at position 78; Y by H at position 89; E by Q at position 107; E by H at position 107; P by A at position 109; L by V at position 110; M by V at position 111; E by Q at position 113; E by H at position 113; L by V at position 117; L by I at position 117; K by Q at position 121; K by T at position 121; R by H at position 125; R by Q at position 125; K by Q at position 133; K by T at position 133; E by Q at position 159 and E by H at position 159.

8. (Currently amended) A modified IFNα-2b or IFNα-2a cytokine of claim [[5]] 6, further comprising ~~proteins comprising one or more sets of~~ [[dual]] duo-amino acid replacements corresponding to replacements in SEQ ID NOS:1 or 182~~, corresponding to~~ selected from among:

D by N at position 2 and P by S at position 4;

D by N at position 2 and P by T at position 4;

L by N at position 3 and Q by S at position 5;

L by N at position 3 and Q by T at position 5;

P by N at position 4 and T by S at position 6;

P by N at position 4 and T by T at position 6;

Q by N at position 5 and H by S at position 7;

Q by N at position 5 and H by T at position 7;

T by N at position 6 and S by S at position 8;

T by N at position 6 and S by T at position 8;

H by N at position 7 and L by S at position 9;

H by N at position 7 and L by T at position 9;

S by N at position 8 and G by S at position 10;

S by N at position 8 and G by T at position 10;

L by N at position 9 and S by S at position 11;

L by N at position 9 and S by T at position 11;

M by N at position 21 and K by S at position 23;

M by N at position 21 and K by T at position 23;

R by N at position 22 and I by S at position 24;

R by N at position 22 and I by T at position 24;

R or K by N at position 23 and S by S at position 25;

R or K by N at position 23 and S by T at position 25;

I by N at position 24 and L by S at position 26;

I by N at position 24 and L by T at position 26;

S by N at position 25 and F by S at position 27;

S by N at position 25 and F by T at position 27;

L by N at position 26 and S by S at position 28;

L by N at position 26 and S by T at position 28;

S by N at position 28 and L by S at position 30;

S by N at position 28 and L by T at position 30;

L by N at position 30 and D by S at position 32;

L by N at position 30 and D by T at position 32;

K by N at position 31 and R by S at position 33;

K by N at position 31 and R by T at position 33;

D by N at position 32 and H by S at position 34;

D by N at position 32 and H by T at position 34;

R by N at position 33 and D by S at position 35;

R by N at position 33 and D by T at position 35;

H by N at position 34 and F by S at position 36;

H by N at position 34 and F by T at position 36;

D by N at position 35 and G by S at position 37;

D by N at position 35 and G by T at position 37;

F by N at position 36 and F by S at position 38;

F by N at position 36 and F by T at position 38;

G by N at position 37 and P by S at position 39;

G by N at position 37 and P by T at position 39;

F by N at position 38 and Q by S at position 40;

F by N at position 38 and Q by T at position 40;

P by N at position 39 and E by S at position 41;

P by N at position 39 and E by T at position 41;

Q by N at position 40 and E by S at position 42;

Q by N at position 40 and E by T at position 42;

E by N at position 41 and F by S at position 43;

E by N at position 41 and F by T at position 43;

E by N at position 42 and G by S at position 44;

E by N at position 42 and G by T at position 44;

F by N at position 43 and N by S at position 45;

F by N at position 43 and N by T at position 45;

G by N at position 44 and Q by S at position 46;

G by N at position 44 and Q by T at position 46;

N by N at position 45 and F by S at position 47;

N by N at position 45 and F by T at position 47;

Q by N at position 46 and Q by S at position 48;

Q by N at position 46 and Q by T at position 48;

F by N at position 47 and K by S at position 49;

F by N at position 47 and K by T at position 49;

Q by N at position 48 and A by S at position 50;

Q by N at position 48 and A by T at position 50;

K by N at position 49 and E by S at position 51;

K by N at position 49 and E by T at position 51;

A by N at position 50 and T by S at position 52;

A by N at position 50 and T by T at position 52;

S by N at position 68 and K by S at position 70;

S by N at position 68 and K by T at position 70;

K by N at position 70 and S by S at position 72;

K by N at position 70 and S by T at position 72;

A by N at position 75 and D by S at position 77;

A by N at position 75 and D by T at position 77;

D by N at position 77 and T by S at position 79;

D by N at position 77 and T by T at position 79;

I by N at position 100 and G by S at position 102;

I by N at position 100 and G by T at position 102;

Q by N at position 101 and V by S at position 103;

Q by N at position 101 and V by T at position 103;

G by N at position 102 and G by S at position 104;

G by N at position 102 and G by T at position 104;

V by N at position 103 and V by S at position 105;

V by N at position 103 and V by T at position 105;

G by N at position 104 and T by S at position 106;

G by N at position 104 and T by T at position 106;

V by N at position 105 and E by S at position 107;

V by N at position 105 and E by T at position 107;

T by N at position 106 and T by S at position 108;

T by N at position 106 and T by T at position 108;

E by N at position 107 and P by S at position 109;

E by N at position 107 and P by T at position 109;

T by N at position 108 and I by S at position 110;

T by N at position 108 and I by T at position 110;

K by N at position 134 and S by S at position 136;

K by N at position 134 and S by T at position 136;

S by N at position 154 and N by S at position 156;

S by N at position 154 and N by T at position 156;

T by N at position 155 and L by S at position 157;

T by N at position 155 and L by T at position 157;

N by N at position 156 and Q by S at position 158;

N by N at position 156 and Q by T at position 158;

L by N at position 157 and E by S at position 159;

L by N at position 157 and E by T at position 159;

Q by N at position 158 and S by S at position 160;

Q by N at position 158 and S by T at position 160;

E by N at position 159 and L by S at position 161;

E by N at position 159 and L by T at position 161;

S by N at position 160 and R by S at position 162;

S by N at position 160 and R by T at position 162;

L by N at position 161 and S by S at position 163;

L by N at position 161 and S by T at position 163;

R by N at position 162 and K by S at position 164;

R by N at position 162 and K by T at position 164;

S by N at position 163 and E by S at position 165; and

S by N at position 163 and E by T at position 165,

wherein residue 1 corresponds to residue 1 of the mature IFNα-2b or IFNα-2a cytokine set forth in SEQ ID NOS:1 or 182.

9. (Currently amended) A modified IFNα-2b or IFNα-2a ~~mutant~~ cytokine of claim [[5]] 6, further comprising ~~selected from proteins comprising one or more sets of~~ [[dual]] duo- amino acid replacements corresponding to replacements in SEQ ID NOS:1 or 182~~, corresponding to~~ selected from among:

Q by N at position 5 and H by S at position 7;

P by N at position 39 and E by S at position 41;

P by N at position 39 and E by T at position 41;

Q by N at position 40 and E by S at position 42;

Q by N at position 40 and E by T at position 42;

E by N at position 41 and F by S at position 43;

E by N at position 41 and F by T at position 43;

F by N at position 43 and N by S at position 45;

G by N at position 44 and Q by T at position 46;

N by N at position 45 and F by S at position 47;

N by N at position 45 and F by T at position 47;

Q by N at position 46 and Q by S at position 48;

F by N at position 47 and K by S at position 49;

F by N at position 47 and K by T at position 49;

I by N at position 100 and G by S at position 102;

I by N at position 100 and G by T at position 102;

V by N at position 105 and E by S at position 107;

V by N at position 105 and E by T at position 107;

T by N at position 106 and T by S at position 108;

T by N at position 106 and T by T at position 108;

E by N at position 107 and P by S at position 109;

E by N at position 107 and P by T at position 109;

L by N at position 157 and E by S at position 159;

L by N at position 157 and E by T at position 159;

E by N at position 159 and L by S at position 161; and

E by N at position 159 and L by T at position 161.

10-15. (Canceled)

16. (Original) A modified cytokine of claim 5 that has increased antiviral activity compared to the unmodified cytokine.

17. (Original) The modified cytokine of claim 16, wherein antiviral activity is assessed by measuring replication by reverse transcription quantification PCR (RT-qPCR).

18. (Previously presented) A modified cytokine of claim 5 that has more antiviral activity than anti-proliferative activity compared to the unmodified cytokine.

19. (Previously presented) The modified cytokine of claim 18, wherein anti-proliferative activity is assessed by measuring cell proliferation in the presence of the cytokine.

20. (Canceled)

21. (Original) A modified cytokine of claim 1, comprising two or more mutations.

22. (Original) The modified cytokine of claim 21 that is a modified IFNα-2b cytokine.

23. (Currently amended) A modified cytokine of claim 1, wherein the cytokine comprises the sequence of amino acids set forth in any of SEQ ID NOS: ~~2 through 181~~ 2-17, 19-131, 134-181, 978-988 or 1303 wherein the arginine at position 23 is replaced with a lysine.

24-39. (Canceled)

40. (Original) A pharmaceutical composition, comprising a cytokine of claim 1 in a pharmaceutically acceptable carrier.

41-42. (Canceled)

43. (Previously presented) A modified cytokine of claim 1 that is a structural homolog of IFNα-2b, comprising one or more amino acid replacements in the cytokine structural homolog at positions corresponding to the 3-dimensional-structurally-similar modified positions within the 3-D structure of the modified IFNα-2b, IFNα-2a, IFNα-2c or an interferon of SEQ ID NO: 232.

44. (Original) A modified cytokine of claim 43, wherein the homolog has increased resistance to proteolysis compared to its unmodified cytokine counterpart, wherein the resistance to proteolysis is measured by mixture with a protease *in vitro*, incubation with blood or incubation with serum.

45. (Canceled)

46. (Currently amended) The cytokine of claim [[45]] 44, selected from among IFNα-2a, IFNα-c, IFNα-2c, IFNα-d, IFNα-5, IFNα-6, IFNα-4, IFNα-4b, IFNα-I, IFNα-J, IFNα-H, IFNα-F, IFNα-8, and IFNα-consensus cytokine.

47. (Previously presented) A modified cytokine of claim 1 that is modified IFNα-2a cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 182 in the IFNα-2a corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of unmodified IFNα-2b, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or a with a blood lysate or by incubation with serum, compared to the unmodified IFN alpha-2a.

48. (Previously presented) The modified IFNα-2a of claim 47, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 182, corresponding to amino acid positions 41, 58, 78, 107, 117, 125, 133 and 159.

49. (Previously presented) A modified IFNα-c cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 183 in the IFNα-c corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFN alpha-c.

50. (Previously presented) The modified IFNα-c of claim 49, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 183, corresponding to amino acid positions 41, 59, 79, 108, 118, 126, 134 and 160.

51. (Previously presented) A modified IFNα-c, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 185 in the IFNα-2c corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-2c.

52. (Previously presented) The modified IFNα-2c cytokine of claim 51, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 185, corresponding to amino acid positions 27, 33, 41, 58, 78, 89, 107, 109, 110, 111, 113, 117, 121, 125, 133 and 159.

53. (Previously presented) A modified IFNα-d cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 186 in the IFNα-d corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-d.

54. (Previously presented) The IFNα-d modified cytokine of claim 53, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 186, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111, 112, 114, 118, 122, 126, 134 and 160.

55. (Previously presented) A modified IFNα-5 cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 187 in the IFNα-5 corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-5.

56. (Previously presented) The IFNα-5 modified cytokine of claim 55, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 187, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

57. (Previously presented) A modified IFNα-6 cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 188 in the IFNα-6 corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-6.

58. (Previously presented) The IFNα-6 modified cytokine of claim 57, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 188, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111, 112, 114, 118, 122, 126, 134 and 160.

59. (Previously presented) A modified IFNα-4 cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 189 in the IFNα-4 corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-4.

60. (Previously presented) The IFNα-4 modified cytokine of claim 59, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 189, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111, 112, 114, 118, 122, 126, 134 and 160.

61. (Previously presented) A modified IFNα-4b cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 190 in the IFNα-4b corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-4b.

62. (Previously presented) The IFNα-4b modified cytokine of claim 61, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 190, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111, 112, 114, 118, 122, 126, 134 and 160.

63. (Previously presented) A modified IFNα-I cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 191 in the IFNα-I corresponding to a structurally-related modified amino acid position within the 3-dimensional

structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-I.

64. (Previously presented) The IFNα-I modified cytokine of claim 63, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 191, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

65. (Previously presented) A modified IFNα-J cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 192 in the IFNα-J corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-J.

66. (Previously presented) The IFNα-J modified cytokine of claim 65, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 192, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

67. (Previously presented) A modified IFNα-H cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 193 in the IFNα-H corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-H.

68. (Previously presented) The IFNα-H modified cytokine of claim 67, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 193, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

69. (Previously presented) An IFNα-F cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 194 in the IFNα-F corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-F.

70. (Previously presented) The IFNα-F modified cytokine of claim 69, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 194, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

71. (Previously presented) An IFNα-8 cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 195 in the IFNα-8 corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-8.

72. (Previously presented) The IFNα-8 modified cytokine of claim 71, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 195, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

73. (Previously presented) An IFNα-consensus cytokine, comprising one or more amino acid replacements at one or more target positions in SEQ ID NO: 232 in the IFNα-consensus cytokine corresponding to a structurally-related modified amino acid position within the 3-dimensional structure of IFNα-2b modified cytokines of claim 5, wherein the replacements lead to greater resistance to proteases, as assessed by incubation with a protease or with a blood lysate or by incubation with serum, compared to the unmodified IFNα-consensus.

74. (Previously presented) The modified cytokine of claim 1 that is an IFNα-consensus cytokine, that is human and is selected from cytokines comprising one or more single amino acid replacements in SEQ ID NO: 232, corresponding to amino acid positions 27, 33, 41, 59, 79, 90, 108, 110, 111,112, 114, 118, 122, 126, 134 and 160.

75-138. (Canceled)

139. (Original) The modified IFNα-2b cytokine of claim 5 that has increased stability compared to the unmodified cytokine, wherein stability is assessed by measuring residual biological activity to either inhibit viral replication or to stimulate cell proliferation in appropriate cells, after incubation with either mixtures of proteases, individual proteases, blood lysate or serum.

140. (Original) The modified IFNα-2b cytokine of claim 5 that has decreased stability compared to the unmodified cytokine, wherein stability is assessed by measuring

residual biological activity to either inhibit viral replication in the appropriate cells or to stimulate cell proliferation of the appropriate cells, after incubation with either mixtures of proteases, individual proteases, blood lysate or serum.

141. (Original) The modified IFNα-2b cytokine of claim 5 that has increased biological activity compared to the unmodified cytokine, wherein activity is assessed by measuring the capacity to either inhibit viral replication in the appropriate cells or to stimulate cell proliferation of the appropriate cells, after incubation with either mixtures of proteases, individual proteases, blood lysate or serum.

142. (Original) The modified IFNα-2a cytokine of claim 47 that has increased stability compared to the unmodified cytokine, wherein stability is assessed by measuring residual biological activity to either inhibit viral replication or to stimulate cell proliferation in appropriate cells, after incubation with either mixtures of proteases, individual proteases, blood lysate or serum.

143. (Original) The modified IFNα-2a cytokine of claim 47 that has decreased stability compared to the unmodified cytokine, wherein stability is assessed by measuring residual biological activity to either inhibit viral replication in the appropriate cells or to stimulate cell proliferation of the appropriate cells, after incubation with either mixtures of proteases, individual proteases, blood lysate or serum.

144. (Original) The modified IFNα-2a cytokine of claim 47 that has increased biological activity compared to the unmodified cytokine, wherein activity is assessed by measuring the capacity to either inhibit viral replication in the appropriate cells or to stimulate cell proliferation of the appropriate cells, after incubation with either mixtures of proteases, individual proteases, blood lysate or serum.

145-278. (Canceled)

279. (Currently amended) A modified cytokine of claim 1 selected from ~~the group consisting of~~ among modified cytokines comprising a sequence of amino acids set forth in any of SEQ ID NOS: 2-181, ~~233-1303~~ 978-988 or 1303 or [[a]] an interferon alpha structural homolog thereof.

280-305. (Canceled)

306. (Previously presented) A modified cytokine of claim 1 that is an IFNα-2b, IFNα-2a, IFN-2c cytokine selected from proteins comprising one or more single amino acid replacements corresponding to the replacement of: N by D at position 45; D by G at position 94; G by R at position 102; A by G at position 139; or any combination thereof.

307. (Previously presented) A modified cytokine of claim 1 that is an IFNα-2b, IFNα-2a, IFNα-2c cytokine selected from proteins comprising one or more single amino acid replacements in any of SEQ ID NOS: 1, 182, 185 or 232 or any combination thereof corresponding to the replacement: L by V at position 3; L by I at position 3; P by S at position 4; P by S at position 4; P by A at position 4; R by H at position 12; R by Q at position 12; R by H at position 13; R by Q at position 13; M by V at position 16; M by I at position 16; R by H at position 22; R by Q at position 22; R or K by H at position 23; R or K by Q at position 23; F by I at position 27; F by V at position 27; L by V at position 30; L by I at position 30; K by Q at position 31; K by T at position 31; R by H at position 33; R by Q at position 33; E by Q at position 41; E by H at position 41; K by Q at position 49; K by T at position 49; E by Q at position 58; E by H at position 58; K by Q at position 70; K by T at position 70; E by Q at position 78; E by H at position 78; K by Q at position 83; K by T at position 83; Y by H at position 89; Y by I at position 89; E by Q at position 96; E by H at position 96; E by Q at position 107; E by H at position 107; P by S at position 109; P by A at position 109; L by V at position 110; L by I at position 110; M by V at position 111; M by I at position 111; E by Q at position 113; E by H at position 113; L by V at position 117; L by I at position 117; R by H at position 120; R by Q at position 120; K by Q at position 121; K by T at position 121; R by H at position 125; R by Q at position 125; L by V at position 128; L by I at position 128; K by Q at position 131; K by T at position 131; E by Q at position 132; E by H at position 132; K by Q at position 133; K by T at position 133; K by Q at position 134; K by T at position 134; Y by H at position 135; Y by I at position 135; P by S at position 137; P by A at position 137; M by V at position 148; M by I at position 148; R by H at position 149; R by Q at position 149; E by Q at position 159; E by H at position 159; L by V at position 161; L by I at position 161; R by H at position 162; R by Q at position 162; K by Q at position 164; K by T at position 164; E by Q at position 165; and E by H at position 165 or any combination thereof, wherein residue 1 corresponds to residue 1 of the mature IFNα-2b or IFNα-2a cytokine set forth in SEQ ID NOS:1 or 182.

308. (Previously presented) A modified cytokine of claim 1 that is an IFNα-2b, IFNα-2a, IFNα-2c cytokine selected from proteins comprising one or more single amino acid replacements in any of SEQ ID NOS: 1, 182, 185 or 232 or any combination thereof corresponding to the replacement L by V at position 3; L by I at position 3; P by S at position 4; P by A at position 4; R by H at position 12; R by Q at position 12; R by H at position 13; R by Q at position 13; M by V at position 16; M by I at position 16; R by H at position 22; R by Q

at position 22; R or K by H at position 23; R or K by Q at position 23; F by I at position 27; F by V at position 27; L by V at position 30; L by I at position 30; K by Q at position 31; K by T at position 31; R by H at position 33; R by Q at position 33; E by Q at position 41; E by H at position 41; K by Q at position 49; K by T at position 49; E by Q at position 58; E by H at position 58; K by Q at position 70; K by T at position 70; E by Q at position 78; E by H at position 78; K by Q at position 83; K by T at position 83; Y by H at position 89; Y by I at position 89; E by Q at position 96; E by H at position 96; E by Q at position 107; E by H at position 107; P by S at position 109; P by A at position 109; L by V at position 110; L by I at position 110; M by V at position 111; M by I at position 111; E by Q at position 113; E by H at position 113; L by V at position 117; L by I at position 117; R by H at position 120; R by Q at position 120; K by Q at position 121; K by T at position 121; R by H at position 125; R by Q at position 125; L by V at position 128; L by I at position 128; K by Q at position 131; K by T at position 131; E by Q at position 132; E by H at position 132; K by Q at position 133; K by T at position 133; K by Q at position 134; K by T at position 134; Y by H at position 135; Y by I at position 135; P by S at position 137; P by A at position 137; M by V at position 148; M by I at position 148; R by H at position 149; R by Q at position 149; E by Q at position 159; E by H at position 159; L by V at position 161; L by I at position 161; R by H at position 162; R by Q at position 162; K by Q at position 164; K by T at position 164; E by Q at position 165; E by H at position 165; N by D at position 45; D by G at position 94; G by R at position 102; and A by G at position 139, wherein residue 1 corresponds to residue 1 of the mature IFNα-2b or IFNα-2a cytokine set forth in SEQ ID NOS: 1 or 182.

309-314. (Canceled)

315. (Previously presented) A modified IFNα-2b or IFNα-2a cytokine of claim 308 that has more antiviral activity than anti-proliferative activity compared to the unmodified cytokine.

316. (Previously presented) The cytokine of claim 315, wherein anti-proliferative activity is assessed by measuring cell proliferation in the presence of the cytokine.

317-331. (Canceled)

332. (New) The modified cytokine of claim 1 that exhibits increased stability compared to the unmodified cytokine.

333. (New) The modified cytokine of claim 332, wherein the cytokine exhibits increased stability to proteases, human blood lysate, or human serum.

334. (New) The modified cytokine of claim 332, wherein increased stability is exhibited *in vivo*.

335. (New) The modified cytokine of claim 1 that exhibits increased protein half-life *in vitro* or *in vivo* compared to the unmodified cytokine.

336. (New) The modified cytokine of claim 1, that exhibits increased resistance to proteolysis by a protease of the gastrointestinal tract.

337. (New) The modified cytokine of claim 1, that exhibits increased resistance to proteolysis by a protease in the serum.

338. (New) The modified cytokine of claim 1, wherein the polypeptide exhibits increased anti-viral and/or anti-proliferative activity compared to the unmodified cytokine.

339. (New) The modified cytokine of claim 1, wherein the protein exhibits comparable anti-viral and/or anti-proliferative activity compared to the unmodified cytokine.

340. (New) The modified cytokine of claim 1, wherein increased resistance to proteolysis is due to replacement of one or more amino acids at target positions in an unmodified protein that increase resistance of digestion of the protein by protease.

341. (New) The modified cytokine of claim 1, comprising a single amino acid replacement corresponding to the replacement in SEQ ID NOS: 1 or 182 of E by Q at position 41.

342. (New) The modified cytokine of claim 340, comprising a single amino acid replacement corresponding to the replacement in SEQ ID NOS: 1 or 182 of E by Q at position 41.

343. (New) The pharmaceutical composition of claim 40, formulated for oral administration.